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QUINE INTELLECTUAL PROPERTY LAW GROUP, P.C.
P O BOX 458
ALAMEDA, CA 94501

EXAMINER	
QAZI, SABIHA NAIM	
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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Paper No. 20040221

Application Number:09/526,802
Filing Date: March 16, 2000
Appellant(s): PARASRAMPURIA ET AL.

Emily Holiday
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed on 11/25/2003.

(1) Real Party in Interest

A statement identifying the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

The brief does not contain a statement identifying the related appeals and interferences which will directly affect or be directly affected by or have a bearing on the decision in the pending appeal is contained in the brief. Therefore, it is presumed that there are none. The Board, however, may exercise its discretion to require an explicit statement as to the existence of any related appeals and interferences.

(3) Status of Claims

The statement of the status of the claims contained in the brief is correct.

(5) Summary of Invention

The summary of invention contained in the brief is deficient because Applicants are explaining more about polymorphic form VI. According to applicants this form was not known to CHENG and was present as impurity. The issue is not that the impurity was not recognized by the prior art as a new polymorphic form VI. Note, that claims are not drawn to polymorphic form VI, which according to applicants, is their invention. Rather claims are drawn to DHEA formulations for example claim 1, recites "A pharmaceutical formulation comprising dehydroepiandrosterone (DHEA), at least 85% of which is present as form 1 polymorph, and at least one pharmaceutical excipient".

Prior art teaches polymorph 1 which is the most stable form of dehydroepiandrosterone. Detecting and identifying the impurities as form VI is not the claimed invention.

(6) Issues

The appellant's statement of the issues in the brief is partially correct.

(7) Grouping of Claims

Claims 1-10 and 36-39 on appeal are in one group.

(8) Claims Appealed

The copy of the appealed claims contained in the Appendix to the brief is correct. Claims 1-10 and 36-39 are pending.

(10) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Claims 1-10 and 36-39 are rejected under 35 U.S.C. 103(a) as being unpatentable over J. Pharm. Sci. (1995), 84(10), 1169-79 (CHANG et al.) in combination of US Patent 5,407,927 (MORALES et al.) and US Patent 5,077,284 (LORIA et al). These references teach formulations, methods and polymorphic forms of dehydroepisterone (DHEA), which embraces Applicant's claimed invention.

CHANG et al. teaches solid-state crystallization of DHEA and its polymorph (forms I-III). The identification of each modification is based on XRPD patterns. See the abstract. Furthermore, it teaches, "In a purity determination study, 5% contamination modification in binary mixtures of several modifications could be detected by use of XRPD. Furthermore, it discloses that polymorph form I is more stable than others. See last two paragraphs in col. 2 on page 1173.

See also last five lines of 1st para in col. 1 on page 1175 where it teaches, "Results of this analysis are shown in Table 2. <u>These results indicate that the purities of forms I to III and S1 are as high as 95%, and X-ray diffraction powder potentially can be employed as a method of estimating the purity of polymorphs of</u>

DHEA. All modifications were prepared as fine powders, and X-ray powder diffraction patterns of mixtures were reproducible".

Instant claims differ from the reference in claiming formulations and method of preparation of specific polymorphic form I of DHEA (at least 85% pure).

LORIA et al. teaches the formulation of DHEA for the treatment of various diseases such as viral infection, AIDS, immune system. See the entire documents especially lines 37-68, col. 1; lines 35-65, col. 3; Table 1, col. 7; lines 37-66, col. 11lines 4-10 and lines 59-66, col. 12.

MORALES et al. teaches the formulation of DHEA see the entire document especially lines 59-68, col. 2; lines 25-58, col. 3 and table 2 in col. 7. Both the US Patents teach the formulation of DHEA for various methods of treatments.

It would have been obvious to one skilled in the art at the time when instant invention was made, to be motivated to prepare additional beneficial preparations and formulations of DHEA, the preparation may contain at least 95% of DHEA and expected to contain especially polymorph form I because this is the most stable form.

One would expect the same results because when the compositions or the formulations of DHEA would be prepared, it would be the same after dissolving in the solvent, no matter what polymorphic form exists in the solid state it will b e always polymorph I as major component because this is the most stable form.

The motivation is provided by the prior art to prepare formulations of DHEA form I polymorph because form I is taught to be more stable. One would expect same properties with the polymorphic form I of DHEA formulation.

C13 NMR in claims for polymorphic form has been considered, but as was said earlier that prior art compound contains polymorph I therefore, in composition and formulation this will not patentability distinct.

It had been held that by changing the form, purity or other characteristics of an old product does not render the novel form patentable where the difference in form, purity or characteristic was inherent in or rendered obvious by the prior art. *In re Cofer*, 53 CCPA (1966) 830, 835, 354 F2d 664, 668, 148 USPQ 268, 271.

In the light of the forgoing discussion, the Examiner's ultimate legal conclusion is that the subject matter defined by the instant claims would have been obvious within the meaning of 35 U.S.C. 103(a).

(11) Response to Argument

Applicant's arguments have been fully considered but they are not persuasive because 95% DHEA is taught by the CHANG reference, MORALES and LORIA teach different formulations of DHEA for the treatment of various diseases. It is important to note that since different polymorphs have different physical and chemical properties, including solubility and dissolution rate, they may exhibit difference in bioavailability. See 5-8 in second column on page 1169 of CHANG.

a. Examiner disagree that cited references provide no motivation. CHANG teaches at least 95% pure DHEA, at the time of invention one skilled in the art would be motivated to purify (more than 95%) and prepare useful stable DHEA formulations for medicinal purposes.

b. Applicant further argues that neither LORIA nor MORALES teach or suggest anything about the DHEA forms present in the formulation disclosed in

these references. Examiner disagree because even if these references does not refer to any polymorph form, CHANG teaches that stable formulation contain form I, because this is the most stable form

c. Furthermore, it teaches that on the basis of dissolution rate results, form I may be a promising modification to improve the bioavailability of DHEA. Forms I-III are monotropic polymorphs with stability decreasing in the order of form I>form II>form III. From six modifications, five (forms II, III, V, S1, S2 and S3) exhibit similar initial dissolution rates, but sixth (form I) dissolves faster than the others.

d. The basis of the arguments is that prior art does not recognize form VI as impurity. If applicants are identifying the impurity in DHEA as polymorph form VI, it does not mean that the DHEA formulation will be different in purity than the prior art.

e. Declaration by Dr. Patrick Stahly was considered but not found persuasive. See section 5 where it states, "None of the analytical techniques used by CHANG to characterize the DHEA polymorph preparations can distinguish between form I and form VI DHEA." Again claims are not directed to identification of impurity, which applicants named as polymorph VI. It does not matter for formulations whether one name the impurity as any name, as form VI given by applicants. Further, Applicant argues that CHANG erroneously believed that X-ray powder diffraction could distinguish all the DHEA. Solid state NMR and other techniques are again for identification and not relevant to the subject matter as claimed.

Further argument in declaration (see section 10) is that "CHANG's X-ray powder diffraction results do not support the conclusion that CHANG's form I preparation was 95% pure. Examiner disagree because CHANG teaches that the results in Table 2 indicate that the purities of forms I to III and S1 are as high as 95%, and X-ray diffraction powder can potentially can be employed as a method of estimating the purity of polymorphs of DHEA. All modifications were prepared as fine powders, and X-ray powder diffraction patterns of mixtures were reproducible".

Further purification of DHEA would have been obvious to one skilled in the art at the time of invention. No criticality and/or unexpected results are seen, presently claimed invention is considered obvious over the prior art of record.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

Sabiha N. Qazi
Primary Examiner
Art Unit 1616

March 1, 2004

Conferees

Badio, Barbara

BARBARA P. BADIO (PH.D
PRIMARY EXAMINER

Padmanabhan, Sreeni

SREENI PADMANABHAN
SUPERVISORY PATENT EXAMINER

LAW OFFICES OF JONATHAN ALAN QUINE
P O BOX 458
ALAMEDA, CA 94501